REMARKS

I. Amendments

Claims 1-10 and 14-22 have been canceled. Claims 25-39 have been added. The newly added claims do not add or constitute new matter. Support for the newly added claims may be found throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 25-39 are pending in the instant application.

II. Objections

The Examiner has objected to claim 12 as being dependent upon a non-elected base claim. As Applicants have canceled claim 12, and none of claims 25-39 are dependent on non-elected base claims, the objection is no longer relevant.

III. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 3-10, 12 and 14-22 under 35 U.S.C. 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claim. Applicants respectfully traverse this rejection.

Specifically, the Examiner claims that while the specification is enabling for a heterozygous knockout mouse comprising a disruption in one copy of the PERK gene exhibiting phenotypic features including increased susceptibility to seizure as compared to wild-type mice, a method of producing such a transgenic mouse by homologous recombination in mouse ES cells, and a cell isolated from the knockout mouse, and a method of using said mouse to screen an agent that ameliorates a phenotype of said mouse, does not reasonably provide enablement for other transgenic and/or knockout animals comprising any disruption in the PERK gene. The Examiner further asserts that the specification is not enabling for a knockout mouse comprising

any disruption in the PERK gene and methods of using said mouse or cells, nor for a transgenic mouse having a homozygous disruption in the PERK gene wherein said mouse dies within 1-2 days.

In view of the cancellation of claims 3-10, 12 and 14-22, the Examiner's rejection of these claims under 35 U.S.C. 35 U.S.C. § 112, first paragraph is moot. Applicants, therefore, respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicants submit that new claims 25-39 fully meet the requirements and are patentable under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 2, 8, 12, 14 and 21 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicants respectfully traverse this rejection.

Regarding claims 1 and 2, the Examiner asserts that the term "selectable marker" renders the claims indefinite as it is unclear how a marker protein can be part of a vector construct. The Applicants disagree, and believe the specification has clearly defined and described the selectable marker and how it would be used in the targeting vector. Applicants further believe that the term is used in the form normally utilized by those of skill in the art. However, as these claims have been canceled, and the new claims recite a selectable marker gene, this aspect of the rejection is no longer relevant.

The Examiner further asserts that the arrangement of the target construct is unclear. Applicants submit that the new claims clearly set forth the relative arrangement of the elements of the targeting construct, rendering the Examiner's rejection moot.

Further, the Examiner asserts that the word "derived" renders claims 8, 12 and 21 indefinite. Applicants respectfully disagree. As can be found, for example, on page 3, lines 17-19 of the instant specification, the term "derived" is clearly defined and therefore not indefinite. Further, one of ordinary skill in the art would know to what the term "derived", in the context of cells and tissues "derived" from a transgenic mouse, relates. In any case, the current claims do not use the term "derived." Newly added claims use the term "isolated," which term is clear and definite. Therefore, the Examiner's rejection is no longer relevant.

Finally, the Examiner has alleged that the term "significant expression" renders claim 14 indefinite in that it is unclear what level of expression is considered to be significant. Although

Applicants disagree, and believe that one of skill in the art would know what level of expression would be considered significant, claim 14 has been canceled. New claims 25-39 no longer recite the term "significant expression."

Applicants submit that new claims 25-39 are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 U.S.C. § 102

Claims 1-5 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Harding *et al.*, 2000, *Molecular Cell,* Vol 5, pp 897-904 ("Hardinig"). Applicants respectfully traverse the rejection.

According to the Examiner, Harding discloses a PERK targeting construct comprising a first polynucleotide homologous to a first portion of the PERK gene, a second polynucleotide sequence homologous to a second portion of the PERK gene, and a selectable marker gene, and method of producing said targeting construct by obtaining said polynucleotides and inserting them into a vector. The Examiner also asserts that Harding discloses a murine embryonic stem cell comprising said construct.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. See MPEP § 2131. Applicants disagree that the teachings of Harding meet each and every limitation as recited in claims 1-5. However, in order to expedite prosecution of the instant application, claims 1-5 have been canceled in favor of new claims 25-27. Therefore, the rejection under 35 U.S.C. § 102 is no longer relevant.

Claims 25-27 recite a targeting construct capable of disrupting a PERK gene and method of producing the targeting construct, and a murine embryonic stem cell transformed with the targeting construct, wherein the targeting construct produces a disruption in the PERK gene which results in increased susceptibility to seizure in a transgenic mouse when heterozygous and one allele does not produce functional PERK protein and results in perinatal lethality in a transgenic mouse when homozygous and two alleles do not produce functional PERK protein, none of which are anticipated by Harding. Harding does not teach or suggest the targeting construct, method of producing the targeting construct, or cells transformed with the construct as recited in the pending claims. More particularly, Harding does not teach or suggest the

disruption, nor the phenotype of increased susceptibility to seizure or perinatal lethality, as is recited in the pending claims.

As the rejection of claims 1-5 is no longer relevant, and new claims 25-39 are not anticipated by the teachings of Harding, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-517.

Respectfully submitted,

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Kelly L. Quast

Kelly L. Quast, Reg. No. 52,141

Deltagen, Inc.
1031 Bing Street
San Carlos, CA 94070
(650) 569-5100